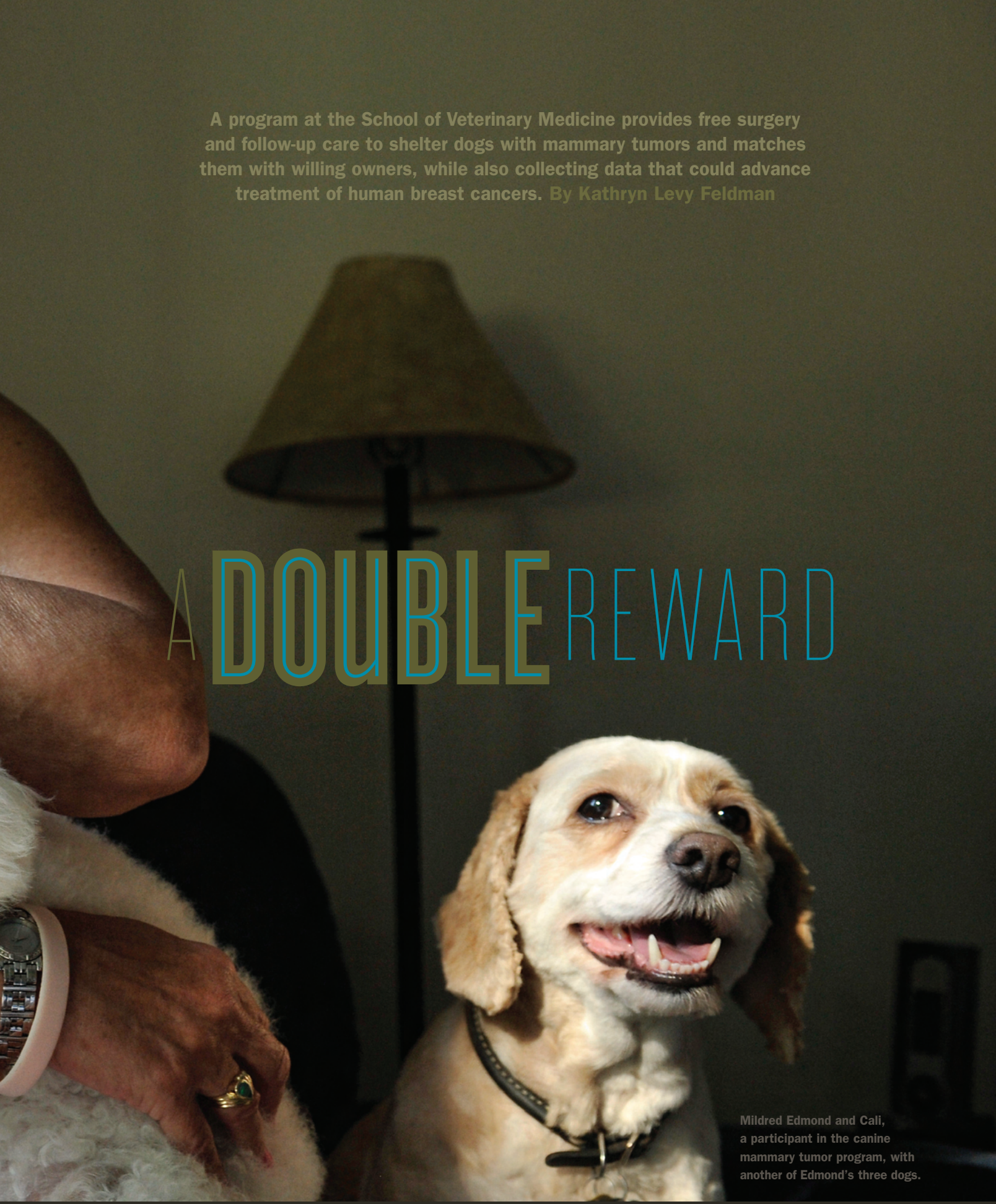
A program at the School of Veterinary Medicine provides free surgery and follow-up care to shelter dogs with mammary tumors and matches them with willing owners, while also collecting data that could advance treatment of human breast cancers. By Kathryn Levy Feldman

A DOUBLE REWARD



Mildred Edmond and Cali, a participant in the canine mammary tumor program, with another of Edmond's three dogs.

PHOTOGRAPHY BY CANDACE DICARLO

"She looked like she needed someone to love her," recalls Mildred Edmond of the first time she saw Cali's picture on the website of the Bucks County, Pennsylvania, SPCA. Edmond already had two dogs—an eight-year-old cock-a-poo and a four-year-old poodle—but like many pet owners her heart is bigger than her house, and she spent a fair amount of time scrolling through the site's list of adoptable dogs. That's what she was doing on the Friday after Thanksgiving 2009, when the image of the six-year-old bichon frise caught her eye.

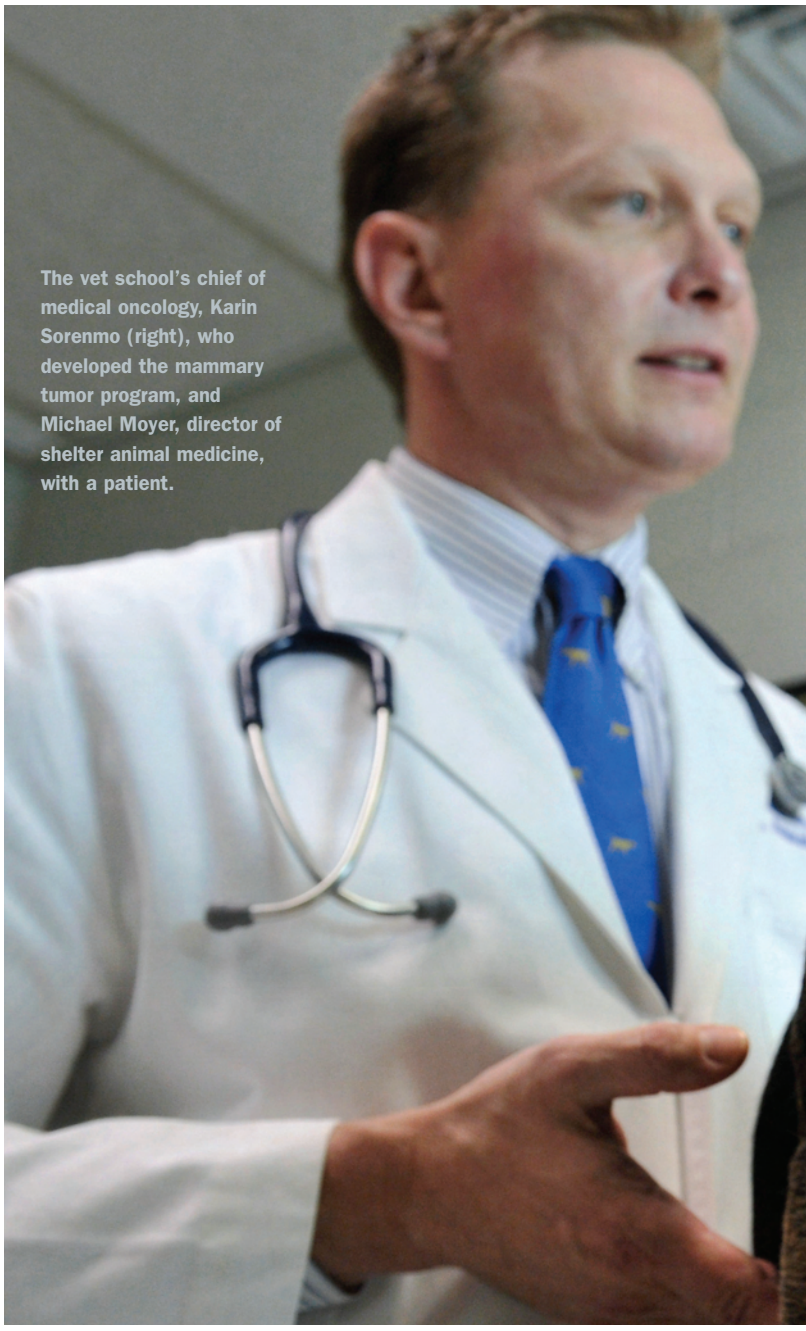
Edmond persuaded her husband to "take a ride, just to look at her," and both were smitten, even after learning about the dog's medical condition. "They told us she had several mammary tumors that would require surgery," Edmond explains. Fortunately, the couple was also told about an innovative program at the School of Veterinary Medicine that would provide the surgery to remove her tumors and follow-up care free of charge. Today Cali, minus her 11 tumors (only one of which was "suspicious"), is one of 17 dogs enrolled in the Penn Vet Shelter Canine Mammary Tumor Program. "We would have adopted her, anyway," says Edmond, herself a survivor of breast and oral cancer. "We knew there were no guarantees about the outcome, but Cali had been neglected. We wanted to make her life comfortable."

The canine mammary tumor program is the brainchild of Karin Sorenmo, chief of medical oncology at the School of Veterinary Medicine, and is designed to provide care for shelter dogs while advancing knowledge about both canine and human breast cancer. "Human breast cancer and mammary tumors in dogs share many similarities in terms of risk factors, biology, and hormone dependence," Sorenmo explains. "We believe that by studying dogs with mammary tumors we can improve our understanding of how cancer develops, and through this understanding find better and more efficient drugs to treat as well as prevent cancer."

Representing the human-medicine side of this collaboration are Robert Vonderheide and Susan Domchek M'05, associate professors and oncologists at the Abramson Cancer Center (as well as husband and wife). Vonderheide, who has been working with Sorenmo for the past six years on the development of a vaccine for lymphoma, calls the venture "an example of the great things that can happen when the School of Medicine works with the vet school—it is after all, 'many species, one medicine,'" in the words of the school's motto.

"There are enough similarities between the species to make the findings relevant," concurs Domchek, whose specialty is breast cancer. "Understanding the risk factors in dogs helps us understand the risk factors in people."

Comparative oncology, a field that integrates the study of naturally occurring cancers in (predominantly companion) animals and research on human cancer biology and therapy, has been around for about 30 years. But the Penn program offers what Sorenmo calls "a double reward," in that knowledge that could advance the understanding and treatment of human cancer is attained not only without harming animals, but by actually saving the lives of some of the most vulnerable members of animal shelter populations. (And, if you ask the grateful owners who have adopted some of these survivors, they would tell you that it's actually a triple reward.)



The vet school's chief of medical oncology, Karin Sorenmo (right), who developed the mammary tumor program, and Michael Moyer, director of shelter animal medicine, with a patient.

Shelter dogs provide an ideal population for studying mammary tumors, because only 10 percent of animals received into shelters have been spayed or neutered. The incidence of mammary tumors in unspayed female dogs is at least four times greater than in spayed dogs. A female dog spayed before she comes into her first heat cycle has only a .5 percent chance of developing a mammary tumor. This is why most veterinarians recommend that female dogs be spayed at a young age if they are not going to be bred.

Few of the dogs referred to Penn's Matthew Ryan Veterinary Hospital for treatment, for example, are unspayed, says Michael Moyer V'90, Rosenthal Director of Shelter Animal Medicine and adjunct associate professor of shelter medicine. "Ninety-five to 99 percent of the female dogs we see have been spayed, which virtually eliminates their risk of developing mammary tumors."

Not so for shelter dogs. Most of these animals have what Moyer calls "a low level of attachment to a household." Many have been acquired by owners who lack the wherewithal to provide regular veterinary care. Many are strays. Most are older (between eight and 10 years), which is when mammary tumors typically develop.

For these reasons, the incidence of mammary tumors in shelter dogs is much higher than in those with permanent owners, and for these dogs the Penn program is a literal lifesaver. "Without surgery, most of these dogs have a low chance of being adopted," says Moyer.

Not all shelter dogs with mammary tumors are accepted into the program. "We screen the candidates and don't do surgery if the cancer has spread to the lungs," explains Sorenmo. "The dogs also have to have good personalities and the shelter has to agree to tell potential owners about the risks associated with adopting a dog with mammary tumors." That said, not all mammary tumors are malignant—although veterinary surgeons do remove all (usually 10) mammary glands. "There is no such thing as 'breast sparing surgery' in dogs," says Sorenmo. "The standard of care is to remove all tumors, regardless of how many and regardless of what stage they are in."

It is precisely the opportunity to examine the development of mammary tumors from non-existent to benign (or pre-malignant) to malignant that makes this study particularly intriguing to oncologists studying human cancers. "In a person, you rarely see progression," says Domchek. "With the dogs, there is so much breast tissue that you get a snapshot of everything at once. You are able to see the entire spectrum of cancer development and search for patterns of gene expres-

SHELTER'S SHIFTING MEANINGS

It's impossible to determine how many stray dogs and cats actually live in the United States. According to the Humane Society, between six and eight million pets end up in shelters each year; three to four million of them are euthanized. (The good news is that about the same number are adopted by new owners—and about 30 percent of shelter dogs, and two to five percent of cats, are reclaimed by their original owners.)

Certainly the need for animal shelters remains strong, especially in areas hard hit by foreclosure and unemployment. "On some weekends we take in more than 100 animals, between owner surrenders and strays," says Gail Luciani, chief officer, public relations and outreach, for the Pennsylvania SPCA.

Modern shelters have evolved considerably from their origins in the "pounds" of 16th-century England. "Many parish churches had a Whipper, whose duty it was to corral unruly dogs that had followed their masters to services. The dogs were kept in a fenced-in area under his supervision," explains Michael Moyer, Rosenthal Director of Shelter Animal Medicine and adjunct associate professor of shelter medicine. "In one parish, the position came with a free flat, so it was a fairly desirable" job. In colonial times, pound masters rounded up and detained wandering livestock until their owners reclaimed them for a fee. "Since these animals had economic value, most farmers were willing to pay the price for their release."

The first animal-welfare organization in the US, the American Society for the Prevention of Cruelty to Animals (ASPCA), was founded in 1866. Initially, its predominant focus was on the mistreatment of horses and other working animals. In 1874, the Philadelphia-based women's branch of the Pennsylvania SPCA became the first animal-welfare organization established to focus on the humane treatment of shelter animals.

They had their work cut out for them.

As the number of free roaming dogs and cats became an issue of public safety (rabies and distemper vaccines were not mandated until the 1960s), cities implemented the pound system to round up strays—most of which were euthanized, frequently by clubbing or drowning, says Moyer.

"Up until the late 1970s, the veterinary community had little input into the management policies of shelters," says Lila Miller, vice president of veterinary outreach at the ASPCA and adjunct assistant professor of shelter medicine. "Instead of focusing on providing humane veterinary care and treatment to the animals, the energies of many shelters revolved around providing a humane death for the many animals that were not reclaimed or adopted."

Further complicating the tensions between animal control and animal welfare, many cities award contracts for animal control to municipal shelters. This model was challenged beginning in 1993, when the San Francisco SPCA relinquished its city-awarded contract for animal control to focus on ending the euthanasia of adoptable animals, giving birth to the "no-kill" movement.

The debate is far from settled and frequently pits open-admission shelters, which must accept every animal, against those that have the means to rehabilitate and re-home the animals they take in. In many ways, however, the dispute has been beneficial. "Despite the rift in the animal welfare community, the result of the debate has been a concerted effort by shelters and communities across the county to reduce the number of adoptable animals that are euthanized by focusing on programs that increase adoptions and reduce relinquishments and the number of unwanted animal births," Miller says.

Veterinarians have played a part in this sea change, as many veterinary schools, including Penn's, have begun to offer courses in shelter medicine. Since 2002, Penn Vet has spayed adoptable dogs in partnership with the city. (Many of the students who spay shelter dogs as part of their junior surgery course end up adopting them.)

In 2006, Moyer began offering a senior elective, Introduction to Shelter Medicine, that includes a surgery rotation. "Fourth-year students get true hands-on experience in all aspects of shelter medicine," he explains. "They do surgeries at the shelters and administer vaccinations and wellness exams as part of the intake protocol." In addition, they cover such topics as pet animal overpopulation, forensic medicine, infectious disease control, behavior problems and evaluations, wellness and animal cruelty, neglect, and hoarding.

The course is the second most popular elective and exposes students to an important aspect of urban veterinary medicine, Moyer adds. "At the very least they handle shelter animals and learn the importance of pro bono work in the practice of any veterinarian."

Along with the emergence of shelter medicine as a career option for veterinarians, another factor helping to raise the quality of veterinary care in animal shelters across the country has been a societal shift in attitudes toward pets that has been evolving over the last century. "We've seen a linear explosion in pet populations in Western countries over the last 40 years," James Serpell, director of Penn's Center for the Interaction of Animals and Society ["Saving the Animal Planet," May|June 2000], recently told *New York* magazine. "People are living more isolated lives, are having fewer children, their marriages aren't lasting. All these things sort of break down to a social network and happen to exactly coincide with the growth in pet populations. I think that what's happening is simply that we're allowing animals to fill the gap in our lives."

At the same time, animal shelters have made concerted efforts to make their animals adoptable. Many now screen pets for behavioral issues and work hard to match animals with suitable owners. Foster and rescue operations for most purebred dogs provide a stable pipeline out of the shelter system. "There has been a larger conversation about the fate of animals in general and dog lovers, in particular, have become engaged," notes Moyer. "Within the last five to 10 years, shelters have finally realized that the public is a market, not the enemy."–*K.L.F.*

sion across the continuum." While doctors don't know yet if these are the same genes, and some histology between dog and human cancer is slightly different, the opportunity to see the full range of cancer development is "amazing," she says.

"Dogs present with multiple tumors in multiple breasts and some are precursors for cancer while others are not," Vonderheide adds. "Women with breast cancer do not present with the full range of lesions that are common in shelter dogs." The fact that the cancer in dogs occurs spontaneously (rather than having been induced in a lab setting) makes it even more relevant. "These are tumors that arise in an outbred, aging mammal exposed to the same environment that we are," he says. "Histologically, these tumors seem to resemble the tumors that humans get."

Traditional funding sources have been slow to recognize the value of such research. "What is almost always misunderstood is that this is not a study on lab animals based on the traditional model of animal studies," says Vonderheide. "We are not inducing cancer; these animals are pets with tumors." At the very least, he says, this study "seems to make the case for NIH funding in the area of comparative oncology. We can learn so much."

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Sorenmo encountered her other collaborator in the mammary tumor program, Olga Troyanskaya, when the Russian-born scientist and dog lover sought her out for advice about treatment for her dog Jessy. Two years ago, her local vet gave the then 13-year-old German shepherd one week to live. Troyanskaya, who is primary investigator at the Princeton University Laboratory for Bioinformatics and Functional Genomics, tracked down Sorenmo at Penn and talked her way into an immediate consultation. Sorenmo recommended a chemotherapy protocol, which extended Jessy's life for six months. In the end, Jessy died from kidney failure, not cancer, and Troyanskaya is grateful for the additional time she got to spend with her beloved pet. "She went from looking like a dog who was going to die to a dog who lived a good quality of life for six months," she says.

It was during those six months of weekly trips to Penn that the two professors began to talk about their respective research. "Somehow the topic came up that I did microanalysis, and we just took it from there," Troyanskaya recalls. Sorenmo, whose interest in breast cancer is personal as well as professional (her mother died of the disease), knew she had found an essential partner in her project.

In her lab at Princeton, Troyanskaya analyzes the molecular composition of the tumor cells removed from the dogs—in particular, the proteins produced by genes as tumors move from pre-malignant to malignant. "Are there any particular groups of genes that seem to be predictable? Why is it that some groupings become malignant and some don't?" she says.

Sorenmo calls Troyanskaya a "superstar," with a track record of being able to find trends in massive amounts of data. Adds Vonderheide, "If anyone can find the needle in the haystack of which gene is changing, she can."

To date, Troyanskaya has tumor profiles from enough dogs to dub the findings "very promising."

"We are able to measure gene expression in dogs and identify genes that are different between normal and tumor cells. We have enough to feel like the signal is there," she elaborates. "The fact that dogs get multiple mammary tumors at the same time makes their genes more similar to those in people than those in mice. We can find groups of genes that are unique to tumors, which is especially exciting because Dog A is just about as different from Dog B as I am from you."

At this point, 17 dogs are enrolled in the study. Two dogs have died, one from cancer and one from unrelated causes. One of the two, Randi, was adopted by Jennifer Wolf despite the advanced stage of her disease. "All I wanted was for her to be in a home, loved and cared for," she says. "The fact that she had cancer made no difference. She, like all shelter dogs, didn't deserve to spend the rest of her life sitting in a shelter."

Jenys Allende, another adoptive owner of a dog enrolled in the program, offers similar sentiments. Allende, a practicing psychiatrist, was already infatuated with Roxy, a cocker spaniel, when she learned the dog had multiple mammary tumors. "We thought she had one or maybe two tumors, but it turned out she had a tumor on almost every mammary gland," she says. "By this point, I knew she was the perfect dog for me, and I wasn't going to give her back." For Allende, everything turned out well. Roxy's biopsies indicated there was no invasive form of cancer. If the situation changes, Allende "will deal with it," she says.

Roxy, like all the dogs in the study, returns to the Ryan Veterinary Hospital for check-ups every four to six months. Most dogs will live two to three years, she estimates, though some will survive longer and others may not make it through the first year. The uncertainty does not seem to faze the owners of the dogs who have been given a second chance. "People have big hearts when it comes to dogs," says Sorenmo. "If the cancer does reoccur, we can give them options for treatment, although the cost for that would not be covered under the study."

One of Sorenmo's longtime goals is to match dogs in the program with more breast cancer survivors like Mildred Edmond. "We know they would be especially vigilant about bringing them back for checkups," she reasons. "Plus it is a very tangible way for them to contribute to groundbreaking research."

Edmond couldn't agree more. "I feel a special bond with Cali probably because I'm a breast cancer survivor myself," she admits. "Maybe we'll get a cure for everything."◆

Kathryn Levy Feldman LPS'09 wrote about Penn's master's degree program in applied positive psychology in the May|June 2010 issue.